FIG. 1

peptide selection

peptide optimization

formation of Fc-peptide DNA construct

insertion of construct into expression vector

transfection of host cell with vector

expression of vector in host cell

Fc multimer formation in host cell

isolation of Fc multimer from host cell-

APPLN. NO: A-527D

FIG. 3A Fc

FIG. 3B

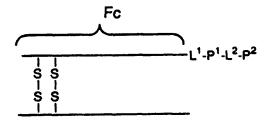


FIG. 3C

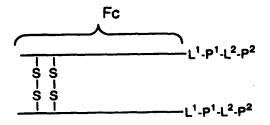
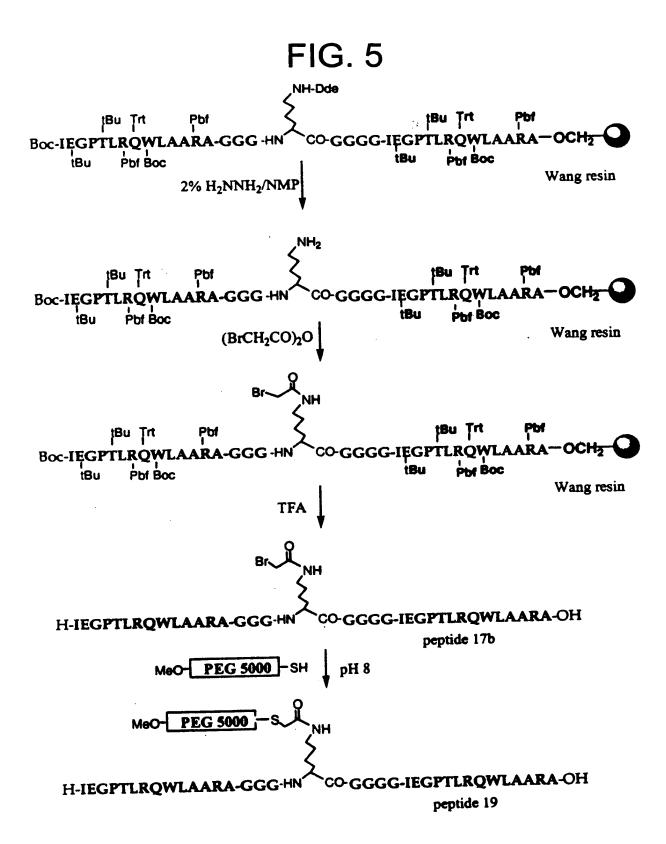


FIG. 4

	•	ATC	3GAC	CAA	AACT	CAC	CAC	ATG:	rcc.	ACC'	l'TG'	rcci	AGC	rcc	3GA2	CTC	CTC	GGG	GGA	CCG	TCA	
	1		CTC	STTI	rtg!	AGT	TG?	raci	\GG	rgg	AAC	AGG	rcg/	AGGG	cri	rgac	GAC	ccc	רכם	GGC	AGT	60
a		М	D	ĸ	T	н	T	С	P	P	С	P	A	P	E	L	L	G	G	P	s	
		GTO	TTC	стс	TTC	ccc	CCA	LAA	ACC	CAAC	GA (CAC	CTC	CATO	SATO	CTCC	CGC	ACC	:CC1	GAG	GTC	
	61		GAAC															-	GG/	CTC	CAG	120
a		v	F	L	F	P	P	ĸ	P	ĸ	D	T	L	M	I	s	R	T	P	E	v	-
		AC/	ATGO	CGTC	GTO	GTO	3GA(CGT	GAG	CAC	:GA	AGA	CC:	rgac	GT(CAAC	STTC	CAAC	TGC	TAC	GTG	
	121		raco	CAC	CAC	CAC	CTO	GCA(•			-+- CCA			- + - 3TTC	GACC	ATC	CAC	180
a		Т	С	v	v	v	D	v	s	н	E	D	P	E	v	ĸ	F	N	W	Y	٧	
		GAG	:GG(CGT	GA(3GT(GCA?	raa:	rgco	CAA	GAC	AAA	3CC	GCG(GGA(GA (GCA(TAC	CAAC	CAGO	CACG	
	181	 Ст(CAC	- + - - CTC	CAC	CGT	+ ATT						CGC		CTY	CGT	CATO	GTT(TCC	TGC	240
a		D	.c	v	E	v	н	N	A	K	T		P		E	E	٥	Y	N	g	т	
•		_	יים. יים	rare	_	• ጉልርረ					-		_		_	_	-	-		GAG	TAC	
	241				-+-			+				+			-+-			+			ATG	300
_		Y		NCA(v	src.	v.	GGA(T	v V	L	н	0	D	W	L	N N	G	K.	E	Y	_
a		-		•	•	_	-	_	_	•			_	_	•••	_		_		_	AGCC	
	301				-+-			+				+			-+-			+			+	360
											_	_		_	_		_:		S	srr. K	rcgg	
a		K	C	K	V 	S	N	K	A	L	P	A	P com	I	E	K smc/	T ccc	I CCN	_	••	A	-
	361				-+-			+				-			-+-			+				420
				_	_			_	TGT						_			_	_	_	CTGG	
a		K	G	Q	P	R	E	P 	Q	-	Y	T 	_	P amm	P	S	R	D CON	E	L ccc	T	•
	421				-+-			+				+			-+-	·		+	• • •		CGTG	480
		TT	CTT	GGT(CCA		•	CTG	_	_							_	_		GCG	GCAC	
a		K	N	Q	V	S	L	T	C	L	v	K	G 	F	Y	P	S 	D Tage	I	A com	V CC 2 C	•
	481				-+-			+				+			- + -			+			GGAC	540
																					CCTG	
a																					D	
	541				-+-			+				+			-+-	• • •		+			GCAG	600
		AG	GCT	GCC	GAG	GAA	GAA	GGA	GAT	GTC	GTT	CGA	GTG	GCA	CCT	GTT	CTC	GTC	CAC	CGT	CGTC	
a		_																			Q	
	601				- 4 -			+				+			-+-			+			GAAG	990
	301	CC	CTT	GCA	GAA	GAG	TAC	GAG	GCA	CTA	CGT	ACT	CCG	AGA	CGI	'GTT	GGT	GAT	GTG	CGT	CTTC	
a		G	N	V	P	S	С	8	V	M	Н	E	A	L	H	N	H	Y	T	Q	K	•
	661		CCT		-+-		• • •	+	·	-	684	•						٠				
		10	- Jun	Unu.						-												

INVENTORS: FEIGE, 6 APPLN. NO: A-527D



TITLE: MODIFIED PEPTIDES AS THERAPEUTIC AGENTS INVENTORS: FEIGE, et al.

APPLN. NO: A-527D

FIG. 6

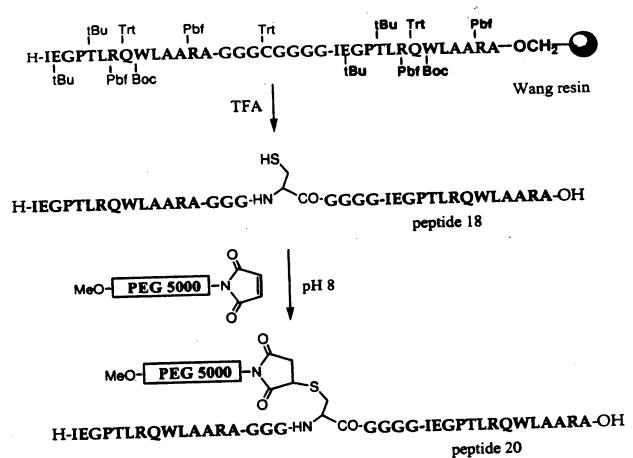


FIG. 7

		XbaI	
c	1	TCTAGATTTGTTTTAACTAATTAAAGGAGGAATAACATATGGACAAAACTCACACATGTC AGATCTAAACAAAATTGATTAATTTCCTCCTTATTGTATACCTGTTTTGAGTGTGTACAG M D K T H T C P	0
c	61	CACCTTGTCCAGCTCCGGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAAC	20
c	121	CCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGA GGTTCCTGTGGGAGTACTAGAGGGCCTGGGGACTCCAGTGTACGCACCACCACCTGCACT K D T L M I S R T P E V T C V V V D V S ·	80
c	181	GCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATG CGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGCACCTCCACGTATTAC H E D P E V K F N W Y V D G V E V H N A -	40
c	241	CCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCA GGTTCTGTTTCGGCGCCCTCCTCGTCATGTTGTCGTGCATGGCACACCAGTCGCAGGAGT K T K P R E E Q Y N S T Y R V V S V L T -	00
c	301	CCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAG GGCAGGACGTGGTCCTGACCGACTTACCGTTCCACGTTCCAGAGGTTGTTTC V L H Q D W L N G K E Y K C K V S N K A	60
c	361	CCCTCCCAGCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCAC GGGAGGGTCGGGGGTAGCTCTTTTGGTAGAGGTTTCGGTTTCCCGTCGGGGCTCTTGGTG L P A P I E K T I S K A K G Q P R E P Q -	20
c	421	AGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCT **TCCACATGTGGGACGGGGTAGGGCCCTACTCGACTGGTTCTTGGTCCAGTCGGACTGGA V Y T L P P S R D E L T K N Q V S L T C -	80
c	481	GCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGC CGGACCAGTTTCCGAAGATAGGGTCGCTGTAGCGGCACCTCACCCTCTCGTTACCCGTCG L V K G F Y P S D I A V E W E S N G Q P	40
c	541	CGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCT GCCTCTTGTTGATGTTCTGGTGCGGAGGGCACGACCTGAGGCTGCCGAGGAAGAAGGAGA E N N Y K T T P P V L D S D G S F F L Y	00
c	601	ACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGGAACGTCTTCTCATGCTCCG TGTCGTTCGAGTGGCACCTGTTCTCGTCCACCGTCGTCCCCTTGCAGAAGAGTACGAGGC S K L T V D K S R W Q Q G N V F S C S V -	60
c	661	TGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTA 7 ACTACGTACTCCGAGACGTGTTGGTGATGTGCGTCTTCTCGGAGAGGGACAGAGGCCCAT M H E A L H N H Y T Q K S L S P G K	20
c	721	AAGGTGGAGGTGGTATCGAAGGTCCGACTCTGCGTCAGTGGCTGCTGCTTCTTTTCCACCTCCACCACCATAGCTTCCAGGCTGAGACGCAGTCACCGACCG	80
	781	BamHİ AATCTCGAGGATCC	

TTAGAGCTCCTAGG

FIG. 8

	Xì	Isc								•		•	•								
		TCTA	GAT	rtg:	TTT	TAAC	CTA	\TT/	LAA C	GAC	GAA	AAT	CAT	ATC	GAC	:AA:	N C	TCA	CAC	ATGTC	
c	1	AGAT	CTA	AAC	AAA	ATT	GAT	'AA'	TTC	CTC	CTI	TTA	GTA	TAC	CTC	TT	rtg.	AGT	GTG'	TACAG C P	
c	61	GTGG	AAC	AGG	TCG	AGG	CT	rgac	GAC	ccc	CCI	GGC	 AGI	CAC	AAC	GA	JAA	+ · ·	GGG	AAAAC TTTTG K P	
c	121	GGTT	CCT	+ GTG(GGA	GTAC	TAC	AGC	GCC	TGC	÷÷	CTC	CAG	TGT	ACC	CAC		+	CCT	CGTGA CGACT	180
	181	GCCA	CGA	AGA(CCC	rgad	GTC	CAAC	TT	AAC	TGG	TAC	GTC	GAC	GGG	GT	GA.	GGT + · ·	GCA	TAATG	240
С		H CCAA	E GAC	D AAA	P GCC	E GCG(V EGAC	K Gac	F SCAC	N TAC	W CAAC	Y :AGC	V ACG	D TAC	G CG1	v Pgt(e Gt	V CAG	H CGT	n a CCTCA	• •
c	241	GGTT	CTG:	rtr	CGG	CGC	CCTC	CTC	CGTC	CATC	TTC	TCG	TGC	ATC	GC.	NCX	CCA	GTC	GCA	GGAGT L T	,
c	301	GGCA	GGA	+ CGT(GGT(CCT	GAC	CGA(TT	CCC	TTC	CTC	ATC	TTC	ACC	TT	CA	+ GAG	GTT	CAAAG GTTTC K A	360
c	361	GGGA	GGG	+ rcg(GGG	GTA	CTC	TT	rtgo	TAC	AGC	TTT	CGG	TT	CCC	GT	CGG	+ GGC	TCT	ACCAC TGGTG	420
c	421	TCCA		+ GTG(GGA		GG1	rag(GCC	CTA	++	GAC	TGG	TTC	TT	GT	CA	+ · · GTC	 GGA	GACCT CTGGA T C	480
c	481	CGGA	CCA	+ GTT	rcc	GAA	GAT	AGG(TC	CTC	TAC	CGG	CAC	CTC	ACC	CT	 CTC	+ GTT	ACC	GCAGC CGTCG Q P	540
c	541		CTT	+ GTT(GAT		CTG	TG	:GG/	\GG(CAC		CTC	AGC	· ·	3CC	GAG	+ Gaa	Gaa	CCTCT + GGAGA L Y	600
c	601	TGTC	GTT	CGA	GTG(GCA	CTC	TTC	CTCC	TCC	CACC	GTC	GTC	CCC	TT	CAC	 3aa	+ GAG	TAC	CTCCG GAGGC S V	660
c	661	ACTA	CGT	··+ ACTY	CCG	AGA	CGT	 3TT(GTO	ATC	TGC	GTC	TTC	TC	GA	GAG	 Gga	+ CAG	AGG	GGGTA CCCAT G K	720
c	721	TTCC	ACC	rcc.	ACC	ACC	ATAG	··· CT	rcc <i>i</i>	 AGGO	· + · · CTGA	AGAC	GC	· + ·	CAC	 CGA	CCG	ACG	AGC	TGCTG ACGAC	780
c	781	GTGG	TGG.	AGGʻ + TCC	TGG	CGG	CGG/	AGG	TAT!	rga(GGC	CCA	ACC	CT	rcg	CA.	ATG TAC	GCT +	TGC	AGCAC TCGTC	840
					В	amH:	I														

GCGCATAATCTCGAGGATCCG 841 + 861 CGCGTATTAGAGCTCCTAGGC c

FIG. 9

		ChaI								ı	1	U		J								
	1	TCTA																		TCTG		^
c	•	AGAT													CTA	CT	rcc.		CTG.	AGAC		U
	61	GTCA		+	• • •	• • •	 .	+		• • • •	+•			• • •			٠	+	• • •	• • • •	+ 1	20
c		_	W	L	A	A	R	A	G	G	G	G	G	G	G	G	I	E	G	P	T ·	
	121	CCCT		+				+ ·	 .		+-			+				+		• • • •	+ 1	80
c		L	R	Q	W	L	A	A	R	A	G	G	G	G	G	D	K	T	Н	T	С -	
c	181	CAGG	TGG	AAC	 GGG	TCG	rgg	ACT1	rgac	GAC	ccc	CCI	rgg	CAG	CA	 \A A	GA	÷ Gaa	GGG		+ 2 T	40
	241	AACC	CAA	GGA	CAC	CCT	CATO	SATO	CTC	CCGC	SACO	CC1	rga(GT	CAC	ATG	CGT	GGT	GGT	GGAC	G .	an
С		TTGG	GTT	CCT	GTG	GGA	GTA (CTAC	3AG(GCC	TGC	:GG/	CT	CAC	itg:	CAC	GCA	CCA	CCA		C	•
	301	TGAG	GGT	··+ GCT	TCT	GGG	ACT	CCAC	GTT(CAAC	+ TTC	SACC	CAT	+ GCA	CT	 GCC	GCA	+ · ·	CCA	CGTA	+ 3 T	60
C		Š ATGC										•							•	H CGTC		
c	361	TACG		CTG	TTT	CGG	CGC	CCT	CCT	CGTC	CATO	TTC	TC	GTG(CAT	GC.	ACA	CCA	GTC		G	20
	421	TCAC		+				+			-+-	· ·		+				+•-			+ 4	80
C			V	L	H	Q	D	W	L	N	G	K	E	Y	K	С	K	V	S	N	K ·	
c	481	TTCG		+ GGG	TCG	GGG	GTA	GCT(CTT	ITG	+- GTA	GAGO	TT	··+ TCG	 GTT	rcc	 CGT	cgg	GGC	• • • •	+ 5 G	
	541	CACA	• • •	+				÷			- + -			+				+			+ 6	00
c		GTGT Q CCTG	V	Y	T	L	P	P	\$	R	D	E	L	T	K	N	Q	V	S	L	T -	
c	601	GGAC	GGA	··+	GTT	TCC	GAA	+ Gat	AGG	GTC	- + - 3CT(JTA(3CG	GCA	CCT	CAC	 CCT	+··	GTT		+ 6	
	661	AGCC	CCT	+ CTT	CTT	GAT	GTT	+ · · CTG	 GTG	CGG	· + - AGG(GCA	CGA	+ CCT	GAG	GCT	GCC	GAG	GAA	GAAG	+ 7 KG	
C		P	E CAG	N CAA	N CCT	Y	K CGT	T GGA	T CAA	P GAG	P CAG	V GTG(L GCA	D GCA	S GGG	D GAA	G CGT	S CTI	F CTC	P ATGC	L - :T	
c	721	AGAT	GTC	+ GTT	CGA	GTG	GCA	+ CCT	 GTT	CTC	· + · GTC	CAC	 CGT	··+ CGT	CCC	CTT	GCA	GAA	GAG	• • • •	+ 7 ia	
	781	CCGT	CTA	+ CGT	ACT	CCG	AGA	+ • • CGT	 GTT	GGT	-+- GAT(GTG(CGT	··+ CTT	CTC	GGA	GAG	÷ GG≀	CAG		+ 8 :C	
c		٧	T-1	n	-	_	u	n	14	**	•	•	~	••	-	_	_	_	-	-		

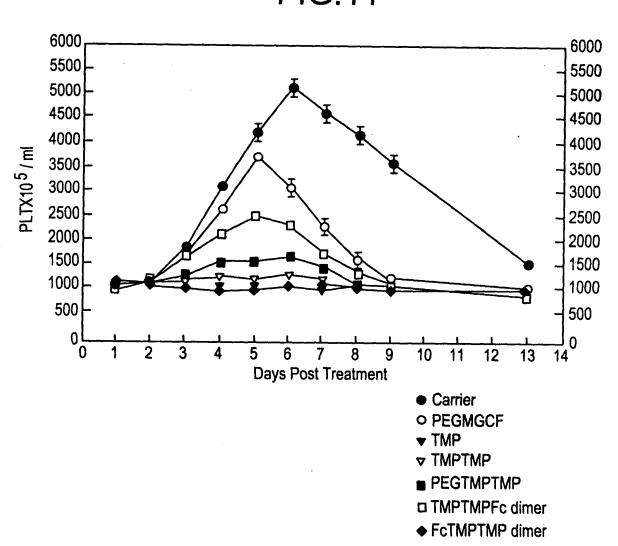
BamHI

C

FIG. 10

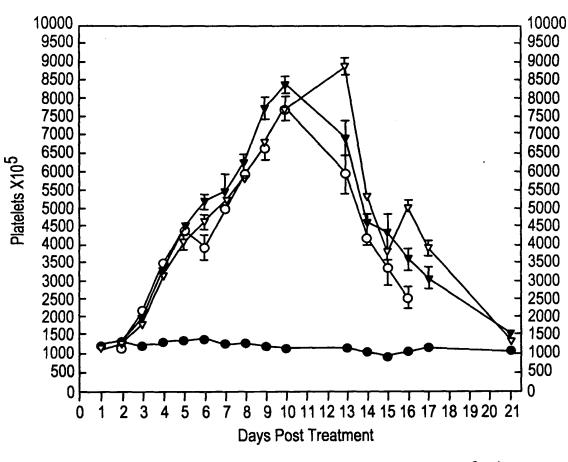
	xbar	
,	TCTAGATTTGTTTTAACTAATTAAAGGAGGAATAACATATGATCGAAGGTCCGACTCTGC	60
1	AGATCTAAACAAAATTGATTAATTTCCTCCTTATTGTATACTAGCTTCCAGGCTGAGACG M I E G P T L R	
	GTCAGTGGCTGCTCGTGCTGGTGGAGGCGGTGGGGACAAAACTCACACATGTCCAC	
61	CAGTCACCGACGACGACGACGACCACCCCGCCACCCTGTTTTGAGTGTGTACAGGTG Q W L A A R A G G G G D R T H T C P P	
	CTTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTTTTCCTCTTCCCCCCAAAACCCA	
121	GAACGGGTCGTGGACTTGAGGACCCCCCTGGCAGTCAAAAGGAGAAGGGGGGTTTTGGGT C P A P E L L G G P S V F L F P P K P K	
	AGGACACCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCC	
181	TCCTGTGGGAGTACTAGAGGGCCTGGGGACTCCAGTGTACGCACCACCACCACCTGCACTCGG	
	DTLMISRTPEVTCVVDVSH	•
241	ACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCA	300
	TGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGCACCTCCACGTATTACGGT E D P E V K F N W Y V D G V E V H N A K	•
	AGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCG	
301	TCTGTTTCGGCGCCCTCCTCGTCATGTTGTCGTGCATGGCACACCAGTCGCAGGAGTGGC	360
	TKPREEQYNSTYRVVSVLTV	•
	TCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGGTGCAAGGTCTCCAACAAAGCCC	420
361	AGGACGTGGTCCTGACCGACTTACCGTTCCTCATGTTCACGTTCCAGAGGTTGTTTCGGG	
	L H Q D W L N G K E Y K C K V S N K A L	•
121	TCCCAGCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG	480
	AGGGTCGGGGGTAGCTCTTTTGGTAGAGGTTTCCGGTTCCCGTCGGGGCTCTTGGTGTCC PAPIEKTISKAKGQPREPQV	•
	TGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGCC	
181	ACATGTGGGACGGGGTAGGGCCCTACTCGACTGGTCCTTGGTCCAGTCGGACTGGACGG	540
	YTLPPSRDELTKNQVSLTCL	•
541	TGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGG	600
744	ACCAGTTTCCGAAGATAGGGTCGCTGTAGCGGCACCTCACCCTCTCGTTACCCGTCGGCC V R G F Y P S D I A V E W E S N G Q P E	
	AGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTACA	
01		660
	N N Y K T T P P V L D S D G S F F L Y S	-
	GCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGA	720
661	CGTTCGAGTGGCACCTGTTCTCGTCCACCGTCGTCCCCTTGCAGAAGAGTACGAGGCACT	
	R L T V D K S R W Q Q G N V F S C S V M	
721	_ •••••································	780
	ACGTACTCCGAGACGTGTTGGTGATGTGCGTCTTCTCGGAGAGGGACAGAGGCCCATTTA H E A L H N H Y T Q K S L S L S P G K *	•
	BamHI	
70-	AATGGATCC	
/8]	1 789 TTACCTAGG	

FIG.11



APPLN. NO: A-527D

FIG.12



- Carrier
- o PEG MGDF
- ▼ TMPTMPFc dimer
- ▼ FcTMPTMP dimer

FIG. 13

3	KbaI								ļ	•		•	•	•						
1	TCTA																		ATGTC	
•	AGAT													CTC		TTG.		GTG:		
61	CACC												GTO	TT	CCT	CTT	CCC	CCC	AAAAC	!
	GTGG/																		TTTTG K P	,
	CCAA																			
121	GGTT	CCT	GTG	GGA(GTA	CTAC	AGC	GCC	TGC	GG?	CTC	CAC	TG	rac	GCA(CÇA	CCA	CCT	GCACT	
	- "	-			M TCN	_	-		-		_		-	_		•	-		V 9	
181			+			4		• • •		+			+ .			•	+	• • •	-	240
	Н																		N A	
241	CCAA																			300
	GGTT(_	_	_		GGAG1 L 1	
	CCGT																			
301		GGA	CGT	GGT	CCT	BACC	CGAC	CTT	ACC	TT	CTC	ATC	TTC	CAC	GTT	CCA	GAG	GTT	GTTTC	;
	V	L	H	Q	D	W	L	N	G .	K	E	Y	K	С	K	V	S	N	K A	٠.
	CTCCC		+		• • •	+	 -	• • • •	• • • ·	+-			-+	• • •	• • •		+	• • •	+	
						-											_	_	rggre P C	
421	AGGT					_		-											GACCT	
421	TCCA	CAT	GTG	GGA	CGG	GGT	PAG	GCC	CTI	CTC	GAC	TG	TT:	CTT	GGT	CCA	GTC	GGA	CTGGA	
		_													_				GCAGO	
481	CGGA	CCA	GTT	TCC		GAT	AGGG	STC	CT(TAC	CGG	CAC	CTC	CAC	CCT	CTC	GTT	ACC	CGTCG	
F 4.1	CGGA				F CAA				D rcc		A SCTO						N CTT		Q F	
541	GCCT																		GGAGA L Y	1
	ACAG	CAA	GCTY	CAC	CGTY	GGAG	CAAC	GAG	CAGO	TG	CAC	CAC	GGG	GAA	CGT	CTT	CTC	ATG	CTCCG	3
601	TGTC	GTT	+ CGA	 GTG	GCA	CCT	FF	CTC	GTC	CAC	GTC	GT	- + CCC	CTI	GCA	GAA	+ GAG	TAC	GAGGC	- 660 :
	s	K	L	T	V	D	K	S	R	W	Q	Q	G	N	V	F	3	С	s v	•
661			+				. •			+-			+	• • •			+		GGGT	720
	ACTA M	CGT. H	ACT ⁴	CCG.	AGA(CGT(H	GTT(N	GGT(H	GAT(Y	T T	Q	X K	S	GGA L	S	GGA L	S	P	G F	
774	AAGG	TGG	AGG'	TGG	TGG	rgg	AGG	TAC	TAC	CTC	rtgo	CA	CTT	CGG	ccc	GCT	GAC	TTG	GGTT	r - 780
721	TTCC	ACC'	TCC.	ACC.	ACC.	ACC'	rcc.	ATG	AAT	GAG	AACC	3GT(GAA(GCC	GGG	CGA	CTG	AAC	CCAAI	1
	•	•	•	•	•	_	•		Bami		-		-	-	-	_	-			
	GCAA							TCG'	TGG.	ATC										
781		• • •	+				+	• • •		-+-	- 81	12								

CGTTTGGCGTCCCACCAATTAGAGCACCTAGG
K P Q G G *

C

FIG. 14 XbaI+....+...+ 60 c M G G T Y S C H -ACTTCGGCCGCTGACTTGGGTATGTAAGCCACAAGGGGGTGGGGGAGGCGGGGGGACA · - + - - - - - - - - + - - - - - - + 120 TGAAGCCGGGCGACTGAACCCATACATTCGGTGTTCCCCCACCCCCTCCGCCCCCCTGT F G P L T W V C K P Q G G G G G D c AAACTCACACATGTCCACCTTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTTTTCC TTTGAGTGTGTACAGGTGGAACGGGTCGTGGACTTGAGGACCCCCCTGGCAGTCAAAAGG THTCPPCPAPELLGGPSVFL C TCTTCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCG AGAAGGGGGTTTTGGGTTCCTGTGGGAGTACTAGAGGGCCTGGGGACTCCAGTGTACGC C PPKPKDTLMISRTPEVTC TGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCG 241 300 ACCACCACCTGCACTCGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGC V V D V S H E D P E V K P N W Y V D G C TGGAGGTGCATAATGCCAAGACAAAGCCGGGGAGGAGCAGTACAACAGCACGTACCGTG EVHNAKTKPREEQYNSTYRV-C TGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCA 361 -----+ 420 ACCAGTCGCAGGAGTGGCAGGACGTGGTCCTGACCGACTTACCGTTCCTCATGTTCACGT c V S V L T V L H Q D W L N G K E Y K C K -AGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGC+...+...+ 480 TCCAGAGGTTGTTTCGGGAGGGTCGGGGGTAGCTCTTTTGGTAGAGGTTTCGGTTTCCCG c V S N K A L P A P I E K T I S K A K G Q -AGCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCGGGATGAGCTGACCAAGAACC TCGGGGCTCTTGGTGTCCACATGTGGGACGGGGGTAGGGCCCTACTCGACTGGTTCTTGG C PREPQVYTLPPSRDELTKNQ-**AGGTCAGCCTGACCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGG** TCCAGTCGGACTGGACGGACCAGTTTCCGAAGATAGGGTCGCTGTAGCGGCACCTCACCC V S L T C L V K G F Y P S D I A V R W E -C **AGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACG** 601 -----+ 660 TCTCGTTACCCGTCGGCCTCTTGTTGATGTTCTGGTGCGGAGGGCACGACCTGAGGCTGC S N G Q P E N N Y K T T P P V L D S D G C GCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACG 661 -----+ 720 CGAGGAAGAAGGAGATGTCGTTCGAGTGGCACCTGTTCTCGTCCACCGTCGTCCCCTTGC SPPLYSKLTVDKSRWQQGNV C TCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCT 721 -----+----+ 780 AGAAGAGTACGAGGCACTACGTACTCCGAGACGTGTTGGTGATGTGCGTCTTCTCGGAGA FSCSVMHEALHNHYTQKSLSc BamHI CCCTGTCTCCGGGTAAATAATGGATCC 781 ----- 807 GGGACAGAGGCCCATTTATTACCTAGG

LSPGK

C

TITLE: MODIFIED PEPTIDES AS THERAPEUTIC AGENTS

INVENTORS: FEIGE, et al. APPLN. NO: A-527D

FIG. 15 XbaI ь MGGTYSC CCACTTCGGCCCACTGACTTGGGTTTGCAAACCGCAGGGTGGCGGCGGCGGCGGCGGCGGTGG GGTGAAGCCGGGTGACTGAACCCAAACGTTTGGCGTCCCACCGCCGCCGCCGCCGCCACC b H F G P L T; W V C K P Q G G G G G G TACCTATTCCTGTCATTTTGGCCCGCTGACCTGGGTATGTAAGCCACAAGGGGGTGGGGG ATGGATAAGGACAGTAAAACCGGGCGACTGGACCCATACATTCGGTGTTCCCCCACCCCC ь TYSCHFGPLTWVCKPQGGG. AGGCGGGGGGACAAAACTCACACATGTCCACCTTGCCCAGCACCTGAACTCCTGGGGGG TCCGCCCCCCTGTTTTGAGTGTGTACAGGTGGAACGGGTCGTGGACTTGAGGACCCCCC b GGGDKTHTCPPCPAPELLGG ACCGTCAGTTTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCC TGGCAGTCAAAAGGAGAAGGGGGGTTTTGGGTTCCTGTGGGAGTACTAGAGGGCCTGGGG PSVFLFPPKPKDTLMISRTP b TGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTG 301 -----+ 360 ACTCCAGTGTACGCACCACCACCTGCACTCGGTGCTTCTGGGACTCCAGTTCAAGTTGAC EVTCVVVDVSHEDPEVKPNW ь GTACGTGGACGCGTGGAGGTGCATAATGCCAAGACAAGCCGCGGGAGGAGCAGTACAA CATGCACCTGCCGCACCTCCACGTATTACGGTTCTGTTTCGGCGCCCCTCCTCGTCATGTT b YVDGVEVHNAKTKPREEQYN CAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAA GTCGTGCATGGCACCAGTCGCAGGAGTGGCAGGACGTGGTCCTGACCGACTTACCGTT ь STYRVVSVLTVLHQDWLNGK-GGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTC CCTCATGTTCACGTTCCAGAGGTTGTTTCGGGAGGGTCGGGGGTAGCTCTTTTGGTAGAG b EYRCKVSNKALPAPIEKTIS CAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGA 541 -----+ 600 GTTTCGGTTTCCCGTCGGGGCTCTTGGTGTCCACATGTGGGACGGGGGTAGGGCCCTACT b KAKGQPREPQVYTLPPSRDE-GCTGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACAT 601 -----+ 660 CGACTGGTTCTTGGTCCAGTCGGACTGGACGGACCAGTTTCCGAAGATAGGGTCGCTGTA LTKNQVSLTCLVKGFYPSD·I ь CGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGT 661 -----+ 720 GCGGCACCTCACCCTCTCGTTACCCGTCGGCCTCTTGTTGATGTTCTGGTGCGGAGGGCA AVEWESNGQPENNYKTTPPVь GCTGGACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTG CGACCTGAGGCTGCCGAGGAAGAAGGAGATGTCGTTCGAGTGGCACCTGTTCTCGTCCAC LDSDGSFFLYSRLTVDKSRW ь GCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACAC CGTCGTCCCCTTGCAGAAGAGTACGAGGCACTACGTACTCCGAGACGTGTTGGTGATGTG Q Q G N V F S C S V M H E A L H N H Y T ь BamHI GCAGAAGAGCCTCTCCCTGTCTCCGGGTAAATAATGGATCC CGTCTTCTCGGAGAGGGGACAGAGGCCCATTTATTACCTAGG

OKSLSLS PGK *

b

INVENTORS: FEIGE, et al. APPLN. NO: A-527D

C

C

c

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C

c

c

C

C

C

c

C

FIG. 16 TCTAGATTTGTTTTAACTAATTAAAGGAGGAATAACATATGGACAAAACTCACACATGTC AGATCTAAACAAAATTGATTAATTTCCTCCTTATTGTATACCTGTTTTGAGTGTGTACAG M D K T H T C P

GCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGCGTGGAGGTGCATAATG

181
CGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGCACCTCCACGTATTAC
H E D P E V K F N W Y V D G V E V H N A

CCAAGACAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTCAGCGTCCTCA

241 -----+ 300
GGTTCTGTTTCGGCGCCCTCCTCGTCATGTTGTCGTGCATGGCACACCAGTCGCAGGAGT

K T K P R E E Q Y N S T Y R V V S V L T -

CCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAG

301
GGCAGGACGTGGTCCTGACCGACTTACCGTTCCTCATGTTCACGGTTCCAGAGGTTGTTTC
V L H Q D W L N G K E Y K C K V S N K A

CCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCAC

361
GGGAGGGTCGGGGGTAGCTCTTTTGGTAGAGGTTTCGGTTTCCCGTCGGGGCTCTTGGTG
L P A P I E K T I S K A K G Q P R E P Q

L V K G P Y P S D I A V E W B S N G Q P CGGAGAACAACTACAAGACCACGCCTCCGGTGCTGGACTCCGACGGCTCCTTCTTCCTCT

GCCTCTTGTTGATGTTCTGGTGCGGAGGGCACGACCTGAGGCTGCCGAGGAAGAAGGAGA
BNNYKTTPPVLDSDGSFFLY

TGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGGCCTCTCCCTGTCTCCGGGTA

ACTACGTACTCCGAGACGTGTTGGTGATGTGCGTCTTCTCGGAGAGGGACAGAGGCCCAT

720

M H E A L H N H Y T Q K S L S L S P G K

AAGGTGGAGGTGGCGGAGGTACTTACTCTTGCCACTTCGGCCCACTGACTTTGGTTT

721+ 780
TTCCACCTCCACCACCGCCTCCATGAATGAGAACGGTGAAGCCGGGTGACTGAACCCAAA
G G G G G T Y S C H F G P L T W V C -

BamHI

TGACCTGGGTATGTAAGCCACAAGGGGGTTAATCTCGAGGATCC
841
ACTGGACCCATACATTCGGTGTTCCCCCAATTAGAGCTCCTAGG
T W V C K P Q G G *

TITLE: MODIFIED PEPTIDES AS THERAPEUTIC AGENTS

INVENTORS: FEIGE, et al. APPLN. NO: A-527D

FIG. 17A

[<u>Aat</u>II sticky end] (position #4358 in pAMG21)

- GCGTAACGTATGCATGGTCTCC
- 3' TGCACGCATTGCATACGTACCAGAGG-
- -CCATGCGAGAGTAGGGAACTGCCAGGCATCAAATAAAACGAAAGGCTCAGTCGAAAGACT --GGTACGCTCTCATCCCTTGACGGTCCGTAGTTTATTTTGCTTTCCGAGTCAGCTTTCTGA -
- -GGGCCTTTCGTTTATCTGTTGTTGTCGGTGAACGCTCTCCTGAGTAGGACAAATCCGC--CCCGGAAAGCAAAATAGACAACAACACCCACTTGCGAGAGGACTCATCCTGTTTAGGCG-
- CGGGAGCGGATTTGAACGTTGCGAAGCAACGCCCGGAGGGTGGCGGGCAGGACGCCCGC GCCCTCGCCTAAACTTGCAACGCTTCGTTGCCGGGCCTCCCACCGCCCGTCCTGCGGGCG -
- CATAAACTGCCAGGCATCAAATTAAGCAGAAGGCCATCCTGACGGATGGCCTTTTTGCGT GTATTTGACGGTCCGTAGTTTAATTCGTCTTCCGGTAGGACTGCCTACCGGAAAAACGCA -

AatII

- TTCTACAAACTCTTTTGTTTATTTTTCTAAATACATTCAAATATGGACGTCGTACTTAAC AAGATGTTTGAGAAAACAAATAAAAAGATTTATGTAAGTTTATACCTGCAGCATGAATTG -
- TTTTAAAGTATGGGCAATCAATTGCTCCTGTTAAAATTGCTTTAGAAATACTTTGGCAGC AAAATTTCATACCCGTTAGTTAACGAGGACAATTTTAACGAAATCTTTATGAAACCGTCG -
- GGTTTGTTGTATTGAGTTTCATTTGCGCATTGGTTAAATGGAAAGTGACCGTGCGCTTAC CCAAACAACATAACTCAAAGTAAACGCGTAACCAATTTACCTTTCACTGGCACGCGAATG -
- TACAGCCTAATATTTTTGAAATATCCCAAGAGCTTTTTCCTTCGCATGCCCACGCTAAAC ATGTCGGATTATAAAAACTTTATAGGGTTCTCGAAAAAGGAAGCGTACGGGTGCGATTTG -
- GATAATTATCAACTAGAGAAGGAACAATTAATGGTATGTTCATACACGCATGTAAAAATA CTATTAATAGTTGATCTCTTCCTTGTTAATTACCATACAAGTATGTGCGTACATTTTTAT -
- AACTATCTATATAGTTGTCTTTCTCTGAATGTGCAAAACTAAGCATTCCGAAGCCATTAT TTGATAGATATATCAACAGAAAGAGACTTACACGTTTTGATTCGTAAGGCTTCGGTAATA -
- TAGCAGTATGAATAGGGAAACTAAACCCAGTGATAAGACCTGATGATTTCGCTTCTTTAA ATCGTCATACTTATCCCTTTGATTTGGGTCACTATTCTGGACTACTAAAGCGAAGAAATT -
- TTACATTTGGAGATTTTTTATTTACAGCATTGTTTTCAAATATATTCCAATTAATCGGTG AATGTAAACCTCTAAAAAATAAATGTCGTAACAAAAGTTTATATAAGGTTAATTAGCCAC -
- AATGATTGGAGTTAGAATAATCTACTATAGGATCATATTTTATTAAATTAGCGTCATCAT TTACTAACCTCAATCTTATTAGATGATGATATCCTAGTATAAAATAATTTAATCGCAGTAGTA -
- AATATTGCCTCCATTTTTTAGGGTAATTATCCAGAATTGAAATATCAGATTTAACCATAG TTATAACGGAGGTAAAAAATCCCATTAATAGGTCTTAACTTTATAGTCTAAATTGGTATC -

- -GCAAGTTTTGCGTGTTATATATCATTAAAACGGTAATAGATTGACATTTGATTCTAATAA--CGTTCAAAACGCACAATATATAGTAATTTTGCCATTATCTAACTGTAAACTAAGATTATT-

FIG. 17B

- ATTGGATTTTTGTCACACTATTATATCGCTTGAAATACAATTGTTTAACATAAGTACCTG -
- TAACCTAAAAACAGTGTGATAATATAGCGAACTTTATGTTAACAAATTGTATTCATGGAC -
- -TAGGATCGTACAGGTTTACGCAAGAAAATGGTTTGTTATAGTCGATTAATCGATTTGATT-
- ATCCTAGCATGTCCAAATGCGTTCTTTTACCAAACAATATCAGCTAATTAGCTAAACTAA
- -CTAGATTTGTTTTAACTAATTAAAGGAGGAATAACATATGGTTAACGCGTTGGAATTCGA-
- GATCTAAACAAAATTGATTAATTTCCTCCTTATTGTATACCAATTGCGCAACCTTAAGCT -

<u>Sac</u>II

- -GCTCACTAGTGTCGACCTGCAGGGTACCATGGAAGCTTACTCGAGGATCCGCGGAAAGAA-
- -CGAGTGATCACAGCTGGACGTCCCATGGTACCTTCGAATGAGCTCCTAGGCGCCCTTTCTT-
- -GAAGAAGAAGAAGCCCGAAAGGAAGCTGAGTTGGCTGCCACCGCTGAGCAATA-
- -CTTCTTCTTCTTCGGGCTTTCCTTCGACTCAACCGACGACGGTGGCGACTCGTTAT-
- -ACTAGCATAACCCCTTGGGGCCTCTAAACGGGTCTTGAGGGGTTTTTTGCTGAAAGGAGG-
- -TGATCGTATTGGGGAACCCCGGAGATTTGCCCAGAACTCCCCAAAAAACGACTTTCCTCC-
- -AACCGCTCTTCACGCTCTTCACGC 3'
- -TTGGCGAGAAGTGCGAGAAGTG 5'

[SacII sticky end]

(position #5904 in pAMG21)

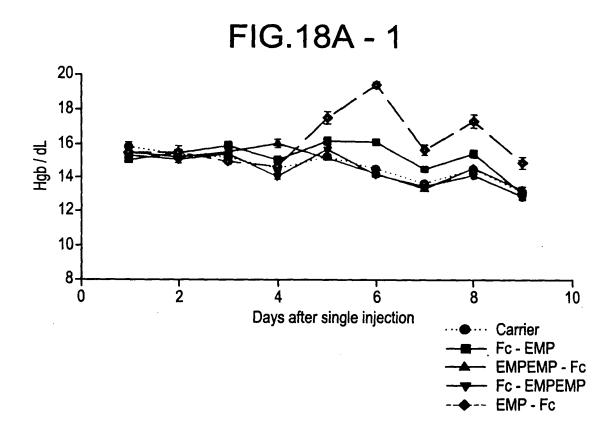


FIG.18A - 2

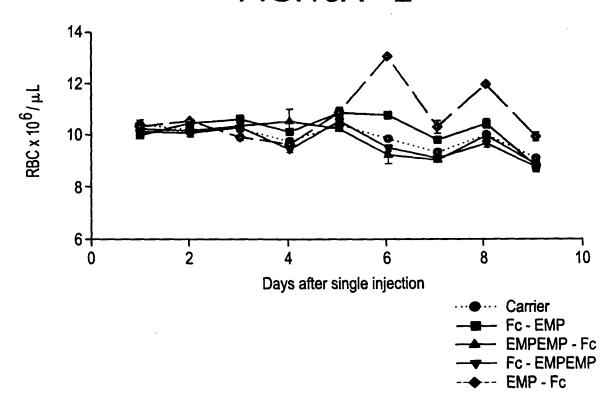


FIG.18A - 3

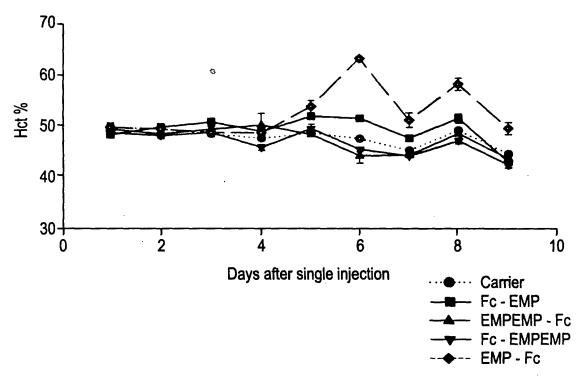


FIG.18B - 1

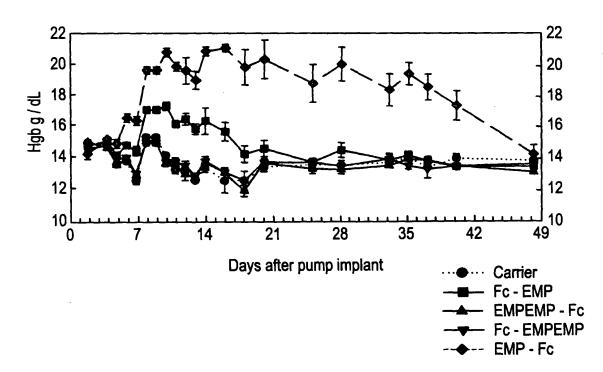


FIG.18B - 2

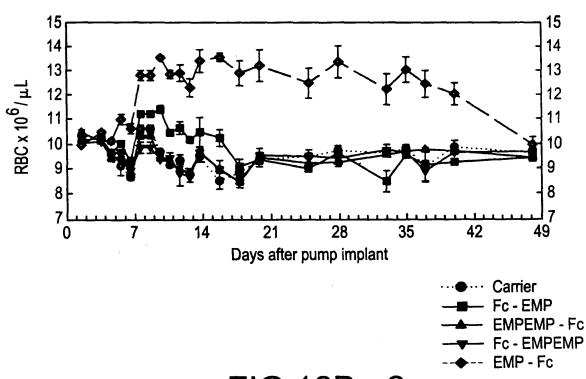
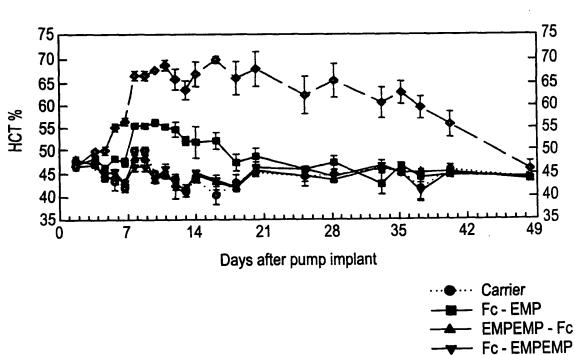


FIG.18B - 3



- EMP - Fc

FIG. 19A NdeI

	_	CA	PAT(GGA	CAA	AAC	TCA	CAC	atg:	rcc <i>i</i>	ACC'	rtg:	rcci	AGC:	rcco	GA	ACTO	CTC	GGG	GGA	CCG	
	1	GT	ATA	CCT	- + - GTT	TTG	AGT	GTG	TAC	AGG	rgg	AAC	AGG	rcg	AGG	CTI	rgac	GAG	ccc	CCI	GGC	60
a			M	D	ĸ	T	н	т	С	P	P	С	P	A	P	E	L	L	G	G	P	•
	61		AGT	CTT	CCT(CTT	ccc	ccci				GGA(CTC	CATO	GATO	CTC	CCG	SAC	CCI	GAG	120
		AG	rca(GAA	GGA(GAA	GGG	GGG'	rtt:	rgg(TT	CTC	GTG	GGA(GTA(CTAC	SAGO	GCC	CTGC	GGA	CTC	
a		S	v	F	L	F	P	P	K	P	ĸ	ם	T	L	M	I	s	R	T	P	E	•
		GT	CAC	ATG											rgad	GT	CAAC	STT	CAAC	TGG	TAC	
	121	CAC	GTG:	TAC				CCT							ACT	CAC	STT	CAAC	STT	ACC	ATG	180
a		v	т	С	v	v	v	D	v	s	н	E	D	P	E	v	ĸ	F	N	W	Y	-
		GT	3GA(CGG	CGT	GGA	GGT	GCA'	raa:	rgco	CAAC	GAC!	AAA(3CC	GCG(GGA(3GA(SCA (STAC	CAAC	CAGC	
	181	CAC	CTC	GCC	- + - 3CA(CCT	CCA	+ CGT				+ CTG1				CT	CCT	+ · CGT(CATO	TTC	TCG	240
a		v	D	G	v	E	v	н	N	A	ĸ	T	ĸ	P	R	E	E	Q	Y	N	s	-
		ACC	<u>ንጥል</u>	ררפי	ኮርጥ	ርርጥ	CAG	ሮርጥ	CCTC	TACO	ገርጥ	רכיזיני	3CA(CAC	iga(<u> </u>	<u> ጉ</u> ርጥ(a A S	rcce	מבר	GAG	
	241	• •	• • •		-+-	• • •	• • •	+	•••	• • •		+			+-	• • •	• • •	+	• • •	• • •	CTC	300
a		T	Y	R	V	V	S	v	L	T	v	L	н	Q	D	W	L	N	G	ĸ	E	-
	301	TAC	CAA	GTG	CAA	GGT	CTC	CAA												CTCC	CAAA	360
		AT	GTT(CAC	GTT	CCA	GAG	GTT	GTT'	rcg	GGA (GGG'	rcg	GGG	GTA(GCT(CTT	rtgo	GTA	GAGC	STTT	
a		Y	K	С	K	V	S	N	K	A	L	P	A	P	I	E	K	T	I	S	K	•
	361	GC	CAA	AGG	GCA	GCC	CCG.	AGA.	ACC.	ACA	GGT	GTA(CAC	CCT	GCC(CCC	ATC	CCG(GGA'	rgac	CTG	420
		CG	GTT'	TCC	CGT	CGG	GGC	TCT'	TGG'	rgte	CCA	CAT	GTG	GGA(CGG	GGG'	rag	GGC(CCT	ACTO	CGAC	
a		A	K	G	Q	P	R	E	P	Q	V	Y	T	L	P	P	3	R	D	E	L	•
	421	AC	CAA	GAA	CCA	GGT	CAG	CCT	GAC	CTG	CCT	GGT	CAA	AGG	CTT	CTA!	rcc	CAG	CGA	CATO	CGCC	480
	421	TG	GTT	CTT	GGT	CCA	GTC	GGA	CTG	GAC	GGA	CCA	GT T	rcc	GAA(GAT	AGG	GTC	GCT	GTAC	GCGG	
a		T	K	N	Q	V	Š	L	T	С	L	v	K	G	F	Y	P	3	D	I	A	•
	404	GT	GGA	GTG	GGA	GAG	CAA	TGG	GCA	GCC	GGA(GAA	CAA	CTA	CAA	GAC	CAC	GCC'	rcc	CGT	GCTG	540
	481	CA	CCT	CAC	CCT	CTC	GTT	ACC	CGT	CGG	CCT	CTT	GTT(GAT(GTT	CTG	GTG	CGG	AGG	GCAC	CGAC	740
a		v	E	W	E	s	N	G	Q	P	E	N	N	Y	K	T	T	P	P	V	L	-
		GA	CTC	CGA	CGG	CTC	CTT	CTT	CCT	CTA	CAG	CAA	GCT	CAC	CGT	GGA	CAA	GAG	CAG	GTG(GCAG	
	541	CT	GAG	GCT	-+- GCC	GAG	GAA	GAA	GGA	GAT	GTC	+ - <i>-</i> GTT	CGA	 GTG	-+- GCA	CCT	GTT	+ CTC	GTC	CAC	+ CGTC	600
a																						

FIG. 19B

	601	• •			-+-			+				+			-+-			+			GCAG + CGTC	660
a		Q	G	N									E								Q	
	661	••			-+-		• • •	+				+			-+-		• • •	+			CTAC + GATG	720
a		ĸ	3	L	S	L	s	P	G	К	G	G	G	G	G	D	F	L	P	н	Y	-
											Ва	I Hmi	•						•			
	721				-+-			+				+	GAT CTA		757	,						
a		ĸ	N	T	s	L	G	Н	R	P	*											

FIG. 20A

		Ņd	еI																		
			ATG	GACT	TCC	TGCC	CGCA	CTA	CAA	AAA	CAC	CTC	TCT	GGG'	TCA	CCG	rcc	GGG'	rggi	AGGC	
	1	GTA	TAC	CTGA	AAGG	ACGO	CGT	'GAT	GTT	TTT	+ GTG	GAG	AGA	CCC.	AGT	GGC	AGG	CCC	ACC'	CCG	60
a			M i	D F	r L	Þ	н	Y	K	N	T	s	L	G	Н	R	P	G	G	G	
	61					CTC															
	91					GAG															120
a		G	G I	D K	(т	н	T	С	P	P	С	P	A	P	E	L	L	G	G	P	-
	121					TCC															100
	121					AGGG															180
a		s	v :	F L	F	P	P	ĸ	P	ĸ	D	T	L	M	I	S	R	T	P	E	-
	101					TGG															240
	191					ACC														CATG	240
a	•	v	T ·	C V	7 V	, v	D	V	s	н	E	D	P	E	V	K	F	N	W	Y	-
						SAGG															
	241																			GTCG	300
a		v	D	G V	/ E	e v	Н	N	A	К	T	к	P	R	E	E	Q	Y	N	s	-
																				GGAG	260
	301					AGT															360
a		T	Y	R V	, v	7 S	v	L	T	v	L	н	Q	D	W	L	N	G	K	E	-
	261														CGA	GAA.	AAC	CAT	CTC	CAAA	420
	361					CAGA									GCT	CTT	TTG	GTA	GAG		420
a		Y	ĸ	C F	k v	, s	N	K	A	L	P	A	P	I	E	K	T	I	S	K	-
	421																			GCTG	480
	421					GGG															400
a		A	K	G () E	R	E	P	Q	V	Y	T	L	P	P	S	R	D	E	L	•
	401	ACC	AAG	AAC	CAGG	STCA	3CC1	GAC	CTG	CCT	GGT	CAA	AGG	CTT	CTA	TCC	CAG	CGA	CAT	CGCC	540
	481	TGG	TTC	TTG	STCC	CAGT	CGG	CTG	GAC	GGA	CCA	GTT	TCC	GAA	GAT	AGG	GTC	GCT	GTA	GCGG	240
a		T	ĸ	N Ç	, ,	<i>7</i> S	L	T	С	L	V	K.	G	F	Y	P	S	D	I	A	-
		GTG	GAG	TGG	GAG	AGCA	ATG	GC.	GCC	GGA	GAA	CAA	CTA	CAA	GAC	CAC	GCC	TCC	CGT	GCTG	601
	541	CAC	CTC	ACC	CTC	rcgt'	raco	CGI	CGG	CCI	CTI	GTI	GAT	GTT	CTG	GTG	CGG	AGG	GCA	CGAC	300
a		٧	E	W I	E 9	3 N	G	Q	P	E	N	N	Y	K	T	T	P	P	v	L	

FIG. 20B

	601			• • •	-+-			+				+ - •			-+-			+			GCAG CGTC	660
a		D	s	D	G	S	F	F	L	Y	S	K	L	T	V	D	K	3	R	W	Q	•
	661				-+-			+				+			-+-			+			GCAG + GCGTC	720
a		Q	G	N	V	F	s	С	s	V	M	Н	E	A	L	Н	N	Н	Y	T	Q	-
	721				CTC -+- GAG			+			ATA	+	GAT		-+-	76	51		•			
_		7.0	~		_			-	_	ש												

FIG. 21A

	No	deI																				
	1	CAT	ATC	GAC						TCC											ACCG	60
		GTA	TAC	CTC	TT	rtg.	AGT	GTG	TAC	AGG	TGG	AAC	AGG	TCG	AGG	CCT	TGA	GGA	ccc	ECC:	rggc	00
a			M	D	K	T	Н	T	С	P	P	С	P	A	P	E	L	L	G	G	Þ	•
	6 1	TCA		TTC											CAT	GAT	CTC	CCG	GAC	cci	rgag	
	01														GTA	CTA	GAG	GGC	CTG	GG/	ACTC	120
a		s	v	F	L	F	P	P	к	P	ĸ	D	T	L	M	ı	s	R	T	P	E	•
	121	• • •			+	• • •		+			· · ·	+			-+-			+		• • • •	STAC CATG	180
a		v						D			н					v			N	W	Y	_
		GTG	GAC	'GGC	'GTG	Ca	GGT!	GCA	ጥልል	_			_	_	_	·		_		 -aac	CAGC	
	181				+			+	·			+	·		-+-			+	· · ·		TCG	240
_																					_	
a.		•	_	G	-	_	·					_		•		_	E	Q	_	N	S	•
	241	• • •			+••		• • •	+				+			-+-			+	·	· • •	GGAG CCTC	300
a		T	Y	R	V	v	s	v	L	T	v	L	н	Q	D	W	L	N	G	ĸ	E	-
																		AAC	CATO	CTC	CAAA	
	301			ACG			_											rtgo	GTA(GAG	GTTT	360
a		Y	ĸ	С	K	v	s	N	ĸ	A	L	P	A	P	I	E	ĸ	T	ı	s	ĸ	-
		GCC	AAA	.GGG	CAC	3CC	CCG.	AGA.	ACC	ACA	GGT	GTA	CAC	CCT	GCC	ccc	ATC	CCG	GGA?	rga(CTG	
	361		TTI	CCC	+·· GTC	 CGG(GGC	+ TCT	TGG	TGT	CCA	+ · · CAT	GTG	GGA	- + - CGG	 GGGʻ	rag(+ GGC(CTI	ACTO	CGAC	420
a		A	K	G	Q	P	R	E	P	Q	V.	Y	T	L	P	P	s	R	D	E	L	
		ACC	AAG	AAC	CAC	GT(CAG	CCT	GAC	CTG	CCT	GGT	CAA	AGG	CTT	CTA'	rcc	CAG	CGA	CATO	CGCC	
	421	TGG	TTC	TTG	+ - ÷	CA	GTC			GAC						GAT	AGG	+ GTC(GCT(STAC	GCGG	480
a																			•		A	
-					_						•										GCTG	
	481				+			+	.			+			-+-	• • •		+		·	GAC	540
_																					L	
a																						
	541				+			+				+			-+-	• • •		+	• • •		GCAG + CGTC	600
a		D	s	D	G	s	F	F	L	Y	s	K	L	Т	V	D	K	S	R	W	Q	•

FIG. 21B

	601	CA	GGG	GAA	CGT	CTT															GCAG	
	001	GT	ccc	CTT	'GCA	GAA															CGTC	
3		Q	G	N	V	F	s	С	s	V	M	н	E	A	L	Н	N	Н	Y	T	Q	-
	661	- •	• • •		-+-			+				+			-+-			+			GGGT + CCCA	720
3		K	S	L	s	L	S	P	G	K	G	G	G	G	G	F	E	W	T	P	G	-
	721				.GCC			+			GTA	+	GAT		-+-		763	ŀ				
		AT	GAC	CGI	'CGG	CAT	'GCG	AGA	CGG	CGA	CAI	TAC	CTA	\GGG	AGC	TC						•
3		Y	W	Q	P	Y	A	L	P	L	*											

FIG. 22A

		- 1	deI						-													
	1	• • •		• • •	- + -		• • •	+				+			-+-			+			AGGC	60
a		GTZ	ATA M	CAA(GCT E	TAC w	CTG T	GGG P													TCCG	
a.				-	_		-	_	G	Y	W	Q	P	Y	A	L	P	L	G	G	G	•
	61				-+-			+				+			-+-			+			ACCG + TGGC	120
a		G	G	D	к	T	н	т	С	P	P	С	P	A	P	E	L	L	G	G	P	
	121				-+-			+				+	·		-+-			+			TGAG + ACTC	180
a		s	v	F	L	F	P	P	ĸ	P	ĸ	D	T	L	M	r	s	R	т	P	E	
	181	• • •			- + -			+				+			-+-			+			GTAC + CATG	240
a		v	T	С	v	v	v	D	V	s	н	E	D	P	E	v	K	F	N	W	Y	•
	241				-+-			+			• • •	+••	•		-+-			+			CAGC + GTCG	300
a		v	D	G	v	E	V	Н	N	A	ĸ	T	K	P	R	E	E	Q	Y	N	s	-
	301				-+-			+				+			-+-			+			GGAG + CCTC	360
a		T	Y	R	v	v	S	v	L	T	v	L	Н	Q	D	W	L	N	G	ĸ	E	
	361				-+-			+				+			-+-			+			CAAA + GTTT	420
a		Y	K	C	ĸ	V	S	N	ĸ	A	L	P	A	P	I	E	ĸ	T	r	s	ĸ	•
	421				-+-			+				+			-+-			+			GCTG + CGAC	480
a		A	ĸ	G	Q	P	R	E	P	Q	v	Y	T	L	P	P	s	R	D	E	L	•
	481		· · · ·		-+-			+				+			-+-	• • •		+			CGCC + GCGG	540
a																				I		-
a					_																GCTG	
	541				-+-			+				+			-+-			+			CGAC	600
a		V	E	W	E	S	N	G	Q	P	E	N	N	Y	K	T	T	P	P	V	L	-

TITLE: MODIFIED PEPTIDES AS THERAPEUTIC AGENTS INVENTORS: FEIGE, et al.

APPLN. NO: A-527D

FIG. 22B

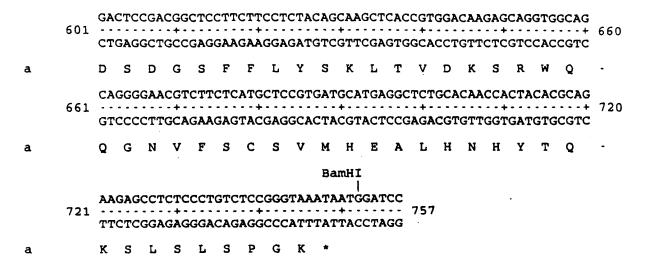


FIG. 23A

	No	leI																				
	1	CATATGGACAAAACTCACACATGTCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCG GTATACCTGTTTTGAGTGTGTACAGGTGGCACGGGTCGTGGACTTGAGGACCCCCCTGGC M D K T H T C P P C P A P E L L G G P TCAGTTTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAG 61															60					
		GTA	TAC	CT	GTT'	TTG.	AGT	GTG'	TAC	AGGʻ	rgg	CAC	GGG'	rcg'	rgg/	ACTI	rgac	GAC	ccc	CCI	rggc	
a			М	D	K	T	н	Т	С	P	P	С	P	A	P	E	L	L	G	G	P	•
	61		. .		-+-			+		-		+			-+-	 .	· ·	-+			TGAG	120
a		s	v	F	L	F	p	P	ĸ	P	ĸ	D	т	L	М	I	s	R	т	P	E.	-
	121				-+-			+				+			-+-			+			GTAC CATG	180
a		V	T	С	V	V	V	D	V	S	H	E	D	P	E	V	K	F	N	W	Y	•
	181				-+-			+				+			-+-			+		· ·	CAGC + GTCG	240
a		v	D	G	v	E	v	н	N	A	ĸ	T	ĸ	P.	R	E	E	Q	Y	N	s	•
	241				-+-			+				+			-+-			+			GGAG CCTC	300
a	•	T	Y	R	v	v	s	v	L	T	v	L	н	Q	D	W	L	N	G	K	E	•
	301				-+-	• • •		+				+			-+-			+			CAAA + GTTT	360
a		Y	K	С	K	V	s	N	K	A	Ļ	P	A	P	I	E	K	T	I	S	K	•
	361				-+-			+				+			-+-			+	• • •	· · ·	GCTG + CGAC	420
a		A	K.	G	Q	P	R	E	P	Q	v	Y	T	L	P	P	s	R	D	E	L	-
	421				-+-			+				+			-+-			+			CGCC + GCGG	480
a		T	ĸ	N	Q	v	s	L	T	С	L	V	ĸ	G	F	Y	P	s	D	I	A	٠
	481	CAC	CT	CAC	-+- CCT	CTC	GTT	ACC	CGT	CGG	CCT	+ CTT	GTT	gat	-+- GTT	CTG	gtg(cgg.	AGG	GCA	CGAC	540
a																					L	
	541				-+-			+				+			-+-			+			GCAG ···+ CGTC	600
a		D	s	D	G	S	F	F	L	Y	S	K	L	T	V	D	K	S	R	W	Q	-

FIG. 23B

	601				-+-			+				+			-+-			+			GCAG + CGTC	660
a		Q	G	N	V	F	S	С	s	V	M	н	E	A	L	Н	N	Н	Y	T	Q	•
	661				-+-			+			• • •	+			-+-	· · ·	· · ·	+			TGAC + ACTG	720
a		K	s	L	s	L	s	P	G	ĸ	G	G	G	G	G	V	E	P	N	С	D	•
		AТ	CCA	TGT	TAT	GTG	GGA	ATG	GGA	ATG	TTT	TGA	ACG	TCI	GTA	ACI	amH CGA	 GGA	TCC	!		
	721	TA	GGT	ACA	-+- ATA	CAC	CCT	TAC	CCT	TAC	AAA	ACI	TGC	AGA	CAT	TGA	GCI	CCI	'AGC	77	3	
a		I	Н	v	M	W	E	W	E	С	F	E	R	L	*							

FIG. 24A

	No	leI																				
	1	CATATGGTTGAACCGAACTGTGACATCCATGTTATGTGGGAATGGGAATGTTTTGAACGT GTATACCAACTTGGCTTGACACTGTAGGTACAATACACCCTTACCATACAAAACTTGCA M V E P N C D I H V M W E W E C F E R CTGGGTGGTGGTGGTGACAAAACTCACACATGTCCACCGTGCCCAGCACCTGAACTC 61 GACCCACCACCACCACCACCACTGTTTTGAGTGTGTACAGGTGGCACGGGTCGTGGACTTGAG																				
		GT?	ATAC	CCA	ACT'	rgg	CTT	GAC.	ACT	GTA	GGT	ACA	ATA	CAC	CCT	raco	CCTT	raca	LAA A	CTI	'GCA	
a				•	_	-	•-	-	_	_		•			_		_	_	-	_		•
	61				- + -			+				+		· · ·	-+-			+ -	· • • •		+	120
a		L	G	G	G	G	G	D	K	T	н	T	С	P	P	С	P	A	p	E	L	-
	121				- + -			+				+			-+-			+ -			TCC AGG	180
a		L	G	G	P	s	v	F	L	F	P	P	K	P	K	D	T	L	M	I	S	-
	181				-+-			+				+			-+-			+		·	CAAG GTTC	240
a		R	T	P	E	v	T	С	v	v	v	D	v	s	H	E	D	P	E	v,	K	-
	241				-+-			+				+			-+-			+		· ·	GAG CCTC	300
a		F	N	W	Y	V	D	G	V	E	V	Н	N	A	K	T	K	P	R	E	E	•
	301				-+-			+			GTC	+ GCA	GGA	GTG	GCA	GGA	CGT	+			GCTG	360
a		Q	Y	N	S	T	Y	R	V	V	S	V	L	T	V	L	н	Q	D	W	L	•
	361				-+-			+				+			-+-			+			GAAA CTTT	420
a		N	G	K	E	Y	K	C	K	V	S	N	K	A	L	P	A	P	I	E	K	•
	421				-+-			+				+		· · ·	-+-			+			ATCC + ragg	480
a		T	I	S	K	A	K	G	Q	P	R	E	P	Q	V	Y	T	L	P	P	S	-
a	481	GC	CCT.	ACT	-+- CGA	CTG	GTI	CTI	GGT	CCA	GTC	+	CTG	GAC	-+- GGA	CCA	GTT	TCC	GAA	GAT	rccc AGGG P	540
u.																					CACG	
	541	TC	GCT	GTA	.GCG	GCA	CCI	CAC	CCI	CTC	GTT	ACC	CGT	CGG	CCT	CTT	GTT	GAT	GTT	CTG	GTGC	600
а		S	D	I	A	V	E	W	E	S	N	G	Q	P	E	N	N	Y	K	T	T	•

FIG. 24B

	601	٠-			-+-			+		• • •	• • •	+			-+-			+			CAAG + GTTC	660
a		P	P	V	L	D	s	D	G	s	F	F	L	Y	S	ĸ	· L	T	V	a	K	-
	661				-+-	• • •		+	• • •			+		• • •	-+-	• • •	• • •	+	• • •		CAAC ···+ GTTG	720
a		s	R	W	Q	Q	G	N	V	F	s	С	s	v	M	н	E	A	L	н	N	-
	721	• •			• + -			+		CCT GGA		+			-+-	ACT		GGA		77	3	
a		Н	Y	T	Q	K	s	L	S	L	s	P	G	K	*							

FIG. 25A

	No	leĮ																				
	1	CAT	ATG	GAC.	AAA +	AC.	rca(CAC	ATG	TCC.	ACC'	TTG' +	TCC.	AGC'	TCC	GGA.	ACTO	CTC	GGG	GGZ	ACCG	60
		GTA	TAC	CTG'	ттт	'TG!	AGT	GTG'	TAC	AGG'	TGG.	AAC.	AGG	TCG.	AGG	CTT	rgac	GAC	ccc	CCI	rggc	•
a			M .	D :	K	T	н	T	С	P	P	С	P	A	P	E	L	L	G	G	P	•
	61	TCA	GTC	TTC	CTC	TT	ccc	ccç.	AAA	ACC	CAA	GGA	CAC	CCT	CAT	GAT	CTC	CGG	SAC	CCI	rgag	
	91	AGT														CTA	SAGO	GCC	CTG	GG.	ACTC	120
a		s	v	F :	L	F	P	P	ĸ	P	ĸ	D	T	L	M	ı	s	R	т	P	E	-
																			CAAC	TGC	STAC	
	121	CAG																	STT(SACC	CATG	180
a		v	T	c '	V	v	v	D	v	s	н	E	D	P	E	v	ĸ	F	N	W	Y	
		GTG	GAC	GGC	GTG	GAG	GT(GCA'	TAA	TGC	CAA	GAC.	AAA	GCC	GCG	GGA(GAG	CAC	STAC	CAAC	CAGC	
	181				+			+				+			-+-			+-				240
•				G 1			v		N		ĸ			P			E		Y	N	s	
a		•	_	_		_	-					_		_		_	_	Q	_	•	_	•
	241			·	+			+				+			-+		· ·	-+-				300
		TGC.	ATG	GCA	CAC	CAC	GTC(GCA(GGA	GTG	GCA(GGA	CGT	GGT(CCT	GAC	CGAC	CTT	ACC	FTTC	CCTC	
a		T	Y	R '	V	V	S	V	L	T	V	L	Н	Q	D.	W	L	N	G	K	E	-
	301			TGC																CTC	CAAA	360
		ATG	TTC.	ACG'	TTC	CAC	GAG	GTT(GTT'	TCG	GGA	GGG	TCG	GGG	GTA	GCT(CTT	rtgo	GTA(A GC	STTT	
a		Y	K	C I	K	V	S	N	K	A	L	P	A	P	I	E	K	T	I	s	K	-
	361		AAA	GGG	CAG	CCC	CG	AGA	ACC.	ACA	GGT	GTA	CAC	CCT	GCC	CCC	ATC	CGG	GA'	GAC	CTG	420
	301		TTT	CCC	GTC	GG	GC'	rct'	TGG	TGT	CCA	CAT	GTG	GGA	CGG	GG'	rago	GC(CT	ACTO	CGAC	420
a		A	ĸ	G (Q	P	R	E	P	Q	v	Y	T	L	P	P	s	R	D	E	L	•
		ACC	AAG.	AAC	CAG	GT	CAG				-										CGCC	400
	421	TGG	TTC	TTG	+ GTC	CAC	GTC														GCGG	480
a		т	K :	N (Q	v	s	L	T	С	L	v	ĸ	G	F	Y	P	s	D	ı	A	•
					_																CTG	
	481				+			+				+			-+-			+ -		. <i>-</i>	GAC	540
																						_
a																					L	
	541				+			+				+			-+-			+ -		• • • ·	SCAG	600
																					CGTC	
2		ח	Q ·	ם מ	G	S	P	P	T.	Y	S	ĸ	τ.	Т	v	D	K	3	R	W	0	-

FIG. 25B

	601				-+-			+				+			-+-			+			GCAG + CGTC	660
3		Q	G	N	V	F	s	C,	s	V	M	Н	E	A	L	Н	N	Н	Y	T	Q	•
	661				-+-			+				+			-+-			+			GGGT CCCA	720
A		K	S	L	Š	L	s	P	G	K	G	G	G	G	G	C	T	T	н	W	G	•
	721				'GTG - + - C A C	СТА		GAT			·	748	S									
a		F	T	L	c	*		•														

FIG. 26A

	No	deI 																				
	1				- + -			+				+			-+-		• • •	+			AGGT + TCCA	60
a			M	С	т	т	н	W	G	F	т	L	С	G	G	G	G	G	D	К	G	
			AGG	CGG'	TGG	GGA	CAA	AAC	TCA	CAC	ATG	TCC	ACC	TTG	CCC	AGC.	ACC'	TGA.	ACT	CCT	GGGG	
	61		rcc	GCC.	- + - ACC	CCT	GTT	+ TTG													CCCC	120
a		G	G	G	G	ם	K	T	н	T	С	P	P	С	P	A	P	E	L	L	G	
	121		. . .		-+-			+				+			-+-			+		. . .	GACC	180
		_	_	_		_		_	_	_		_		_	_						CTGG _	
a		G	P	S	V	F	L 	<i>F</i>	P	P	K	P	K	D	T	L	M	I	3	R	T	•
	181				-+-			+				+			-+-			+	• • •		CAAC + GTTG	240
a		P	E	V	T	С	V	V	V	a	V	S	Н	E	D	P	E	V	K	F	N	-
	241				-+-			+				+			-+-			+			GTAC	300
a		W	¥	v	D	G	v	E	v	н	N	A	K	T	ĸ	P	R	E	E	Q	Y	-
	301			<i>-</i>	-+-			+				+			-+-			+		• • •	TGGC + ACCG	360
a		N	s	T	Y	R	v	v	s	v	L	T	v	L	н	Q	D	W	L	N	G	-
	361				-+-			+				+			-+-			+			CATC ···+ GTAG	420
a		ĸ	E	Y	K	С	ĸ	v	s	N	K ·	A	L	P	A	P	I	E	ĸ	T	I	-
	421				-+-			+	• • • •			+			-+-	• • •		+			GGAT + CCTA	480
a		3	ĸ	A	K	G	Q	P	R	E	P	Q	V	Y	T	L	P	P	Š	R	D	•
	481				-+-			+				+			-+-			+			CGAC + GCTG	540
a		E.	L	T	K	N	Q	v	s	L	T	С	L	v	K	G	F	Y	P	s	מ	-
			CGC	CGT	GGA	.GTG	GGA	GAG	CAA	TGG	GCA	GCC	:GG#	(GAA	CAA	CTA	CAA	GAC	CAC	GCC	TCCC	600
	541	TA	GCG	GCA	CCT	CAC	CCT	CTC	GTI	'ACC	CGT	CGC	CCI	CTI	GTI	GAT	GTT	CTG	GTG	CGG	AGGG	900
		т	a	17	P	W	2	q	N	G	0	P	E	N	N	Y	ĸ	T	т	P	P	-

FIG. 26B

	601	• •			-+-			+				+			-+-			+			CAGG + GTCC	660
3		V	Ł	D	S	D	G	s	F	F	L	Y	s	K	L	T	v	D	ĸ	s	R	•
	661	• •			-+-		• • •	+				+	• • •	• • •	-+-	• • •		+			CTAC	720
3		W	Q	Q	Ģ	N	V	F	S	C	3	V	M	Н	E	A	L	Н	N	Н	Y	•
	721				-+-	CCT		+				+	ATA		GAT		763	i				
3		т	0	K	s	L	s	L	s	P	G	K	*									